thick viscous fat (hot sunshine and sunburns help to thin it and improve it), and they interfere with the polys' ability to destroy acne bacillus so the small pimples get to be big cystic pimples.

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Cimetidine-Associated Thrombocytopenia and Leukopenia

TO THE EDITOR: A brief case report is presented of a 52-year-old man with alcoholic cirrhosis and upper gastrointestinal hemorrhaging, who was treated with intravenous administration of cimetidine on two separate occasions during the same stay in hospital. Leukopenia and thrombocytopenia developed during both treatment periods.

He was admitted to hospital on August 23, 1978, with upper gastrointestinal bleeding. He had consumed no alcohol since July 21, 1978. The findings of a physical examination showed no abnormalities. Laboratory results on admission include the following: leukocyte count, 5,600 per cu mm; hematocrit, 28 percent; prothrombin time, 12.0 seconds (control 10.7 seconds); total protein, 6.0 grams per dl, and serum albumin, 3.4 grams per dl. Total bilirubin, alkaline phosphatase, serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) were within normal limits. Endoscopy disclosed large esophageal varices with adherent clots and erosive duodenitis. The patient was treated with 300 mg of cimetidine, given intravenously every six hours. During the next five days bleeding continued, and a total of eight units of blood was administered. He was given pitressin intravenously and received no other medication. On August 28, he was stable and eating, but the intravenous administration of cimetidine was continued. Two days later the leukopenia and thrombocytopenia were discussed, and cimetidine treatment was stopped (Table 1). On August 31, platelet and leukocyte counts were increased to pretreatment levels. On September 1, 36 hours after administration of cimetidine, a bone marrow

TABLE 1.—*Complete Blood Counts During the Patient's Stay in Hospital*

Date	*Time*	*Leukocytes (per cu mm)*	*Polymorphonuclear Cells (percent)*	*Monocytes (percent)*	*Lymphocytes (percent)*	*Eosinophils (percent)*	*Platelets (per cu mm)*	*Hematocrit (percent)*
8-23-78	18:00	5,600	85	3	11	1	110,000	28
Cimetidine therapy started, 8-23-78								
8-24-78	7:00	2,600	..	..	..	..	55,000	29
8-25-78	7:00	2,900	90	1	9	0	50,000	29
8-25-78	21:15	2,000	..	..	..	..	63,000	23
8-26-78	7:00	2,100	85	2	12	1	45,000	27
8-27-78	7:00	2,500	..	..	..	..	58,000	33
8-27-78	16:30	2,100	80	0	20	0	.....	32
8-28-78	7:00	2,500	79	0	19	2	57,000	33
8-29-78	13:30	2,500	80	5	13	2	22,000	31
8-30-78	7:00	4,300	80	5	13	2	64,000	36
Cimetidine therapy stopped, 8-30-78								
8-31-78	7:00	14,400	92	5	3	0	90,000	33
9- 1-78	7:00	10,000	91	0	9	0	110,000	31
Bone marrow aspiration, 9-1-78								
9- 2-78	15:45	11,100	91	6	3	0	160,000	23
9- 2-78	21:45	14,300	91	5	4	0	173,000	29
9- 3-78	7:00	11,700	..	..	..	..	.....	27
Cimetidine therapy started, 9-3-78								
9- 3-78	22:30	16,600	..	..	..	..	.....	29
9- 4-78	1:30	19,300	..	..	..	..	130,000	34
9- 4-78	10:15	12,100	..	..	..	..	61,000	37
9- 4-78	17:15	10,000	..	..	..	..	48,000	36
9- 4-78	21:00	8,200	..	..	..	..	40,000	35
9- 5-78	6:15	7,200	..	..	..	..	48,000	35
9- 5-78	15:15	5,900	86	3	11	0	.....	32
9- 5-78	19:30	4,700	..	..	..	..	.....	29
9- 6-78	18:15	10,200	..	..	..	..	28,000	34
9- 7-78	7:15	5,000	..	..	..	..	28,000	38
Patient died, 9-9-78								

aspiration was done. Findings included: mild hypercellularity, with mild myeloid hyperplasia with a left shift, mild normoblastic hyperplasia and an adequate number of megakaryocytes. On September 3, upper gastrointestinal hemorrhaging recurred, requiring six units of blood, and a mesocaval shunt was done. After the operation the patient was treated again with intravenous administration of 200 mg of cimetidine every six hours. The following day, platelet and leukocyte counts became depressed (Table 1). Over the next five days encephalopathy developed accompanied by deterioration of liver function test results. The patient died on September 9.

Because of the rapid shifts in the leukocyte and platelet counts, the changes are unlikely to be secondary to bone marrow suppression. The bone marrow aspiration supports this theory. The differential cell count of the bone marrow aspirate was within normal limits, and at no time during the patient's course did the peripheral leukocyte differential shift toward granulocytopenia. No plasma platelet or leukocyte antibodies were obtained. The leukopenia could be secondary to peripheral destruction, redistribution of leukocytes such as margination, or leukocyte sequestration in the body such as splenic sequestration. Possible mechanisms for the thrombocytopenia include platelet sequestration, in vivo platelet aggregation, immune-mediated platelet destruction or disseminated intravascular coagulation. In 1977 Ufberg and co-workers[1] reported a case of a patient with transient leukopenia and neutropenia appearing eight to ten days after beginning oral administration of cimetidine. The condition resolved within 10 to 12 days after stopping the drug. The bone marrow aspirate at that time showed normal cellularity. This was interpreted as being consistent with peripheral destruction of leukocytes and not compatible with bone marrow toxicity.

Except for a study by Posnett and associates[2] in 1979, no previous report of cimetidine-induced leukopenia in the literature had included a rechallenge with the drug. Neutropenia developed in their patient during a 12-day course of high-dose cimetidine (2,400 mg per day). The bone marrow showed hypocellularity compatible with toxic suppression. After a recovery period of three to four weeks, the patient was rechallenged with a standard dose (1,200 mg per day), with no apparent toxicity. They interpreted this as a dose-related, bone marrow toxic suppression. In the present case, the patient was given a second dose of cimetidine and, as with the initial cimetidine therapy, the leukocyte and platelet counts became depressed within 24 hours. This report offers additional evidence for the hematologic effects of cimetidine on the development of leukopenia and, now, thrombocytopenia. But, as previously reported, the myelotoxic potential of cimetidine was not substantiated, and new mechanisms must be considered.

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